

USSN: 10/677,551

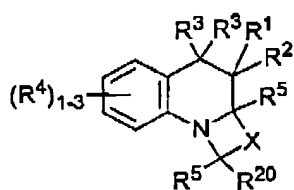
Ref. No. 27712 (formerly 01337.US1)

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound of formula I, including enantiomeric, diastereomeric, or tautomeric isomers thereof, or any pharmaceutically acceptable salt thereof;



I

wherein,

R<sup>1</sup> is

- (a) R<sup>12</sup>
- (b) C(=O)R<sup>6</sup>, or
- (c) CN;

R<sup>2</sup> is

- (a) R<sup>12</sup>
- (b) C(=O)R<sup>7</sup>,
- (c) CN,
- (d) -CH<sub>2</sub>-R<sup>7</sup>,
- (e) -NR<sup>17</sup>R<sup>7</sup>,
- (f) -CH<sub>2</sub>COR<sup>7</sup>,
- (g) -CH<sub>2</sub>CH<sub>2</sub>COR<sup>7</sup>;

Each R<sup>3</sup> is independently

- (a) H,
- (b) R<sup>12</sup>,
- (c) —Oxo,

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

(c) ~~(d)~~ C<sub>1-7</sub> alkyl which is optionally partially unsaturated and is optionally substituted by one or more R<sup>11</sup>,

(d) ~~(e)~~ C<sub>3-8</sub> cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more R<sup>11</sup>,

(e) ~~(f)~~ aryl optionally substituted by one or more R<sup>8</sup>,

(f) ~~(g)~~ heteroaryl optionally substituted by one or more R<sup>8</sup>, or

(g) ~~(h)~~ halo, or

(h) both R<sub>3</sub> taken together are oxo;

Each R<sup>4</sup> is independently

- (a) H,
- (b) halo,
- (c) OR<sup>12</sup>,
- (d) OC(=O)NR<sup>9</sup>R<sup>10</sup>,
- (e) SR<sup>12</sup>,
- (f) S(O)<sub>m</sub>R<sup>13</sup>,
- (g) NR<sup>9</sup>R<sup>10</sup>,
- (h) NR<sup>9</sup>S(O)<sub>m</sub>R<sup>13</sup>,
- (i) NR<sup>9</sup>C(=O)OR<sup>13</sup>,
- (j) phenyl optionally substituted by one or more R<sup>8</sup>,
- (k) heteroaryl optionally substituted by one or more R<sup>8</sup>,
- (l) cyano,
- (m) nitro,
- (n) CONR<sup>9</sup>R<sup>10</sup>,
- (o) CO<sub>2</sub>R<sup>12</sup>,
- (p) C(=O)R<sup>13</sup>,
- (q) C(=NOR<sup>12</sup>)R<sup>13</sup>,
- (r) S(O)<sub>m</sub>NR<sup>9</sup>R<sup>10</sup>,
- (s) NR<sup>9</sup>C(=O)-R<sup>12</sup>,
- (t) C<sub>1-7</sub>alkyl which is optionally partially unsaturated and is optionally substituted by one or more R<sup>11</sup>,

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

(u)  $C_{3-8}$ cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more  $R^{11}$ ,

(v)  $N_3$ ,

(w) het<sup>1</sup> optionally substituted by one or more  $R^8$ , or

(x)  $C(O)O-C_{1-4}$ alkyl- $R^{12}$ ;

Each  $R^5$  is independently,

(a) H,

(b)  $C_{1-7}$ alkyl which is optionally partially unsaturated and is optionally substituted by one or more  $R^{11}$ ,

(c)  $C_{3-8}$ cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more  $R^{11}$ ,

(d) aryl optionally substituted by one or more  $R^8$ , or

(e) heteroaryl optionally substituted by one or more  $R^8$ ;

$R^6$  and  $R^7$  are independently;

(a)  $OR^{12}$ ,

(b)  $NR^9R^{10}$ ,

(c)  $R^{13}$ , or

(e)  $R^6$  and  $R^7$  together with the 2 carbons to which they are attached form cyclohexane-1,3-dione optionally substituted by one or more  $R^{13}$ , cyclopentane-1,3-dione optionally substituted by one or more  $R^{13}$ ,  $R^6$  and  $R^7$  together form  $-N(R^{17})-S(O)_m-N(R^{17})-$ ,  $-N(R^{17})-C(O)-N(R^{17})-$ ,  $-N(R^{17})-C(S)-N(R^{17})-$ ,  $-N(R^{17})-N(R^{17})-$ ,  $-N(R^{17})-C(O)-$ , or  $-N(R^{17})-$ , or  $R^6$  and  $R^7$  together form a phenyl ring;

$R^8$  is

(a) H,

(b) halo,

(c)  $OR^{12}$ ,

(d)  $OCF_3$ ,

(e)  $SR^{12}$ ,

(f)  $S(O)_mR^{13}$ ,

(g)  $NR^9R^{10}$ ,

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

- (h)  $\text{NR}^9\text{S(O)}_m\text{R}^{13}$ ,
- (i)  $\text{NR}^9\text{C(=O)OR}^{13}$ ,
- (j) phenyl optionally substituted by halo, cyano,  $\text{C}_{1-7}$ alkyl, or  $\text{C}_{1-7}$ alkoxy, in the alkyl portion of the  $\text{C}_{1-7}$ alkyl and  $\text{C}_{1-7}$ alkoxy is optionally substituted by one or more  $\text{R}^{11}$ ;
- (k) heteroaryl optionally substituted by halo,  $\text{C}_{1-7}$ alkyl, or  $\text{C}_{1-7}$ alkoxy,
- (l) cyano,
- (m) nitro,
- (n)  $\text{CONR}^9\text{R}^{10}$ ,
- (o)  $\text{CO}_2\text{R}^{12}$ ,
- (p)  $\text{C(=O)R}^{13}$ ,
- (q)  $\text{C(=NOR}^{12})\text{R}^{13}$ ,
- (r)  $\text{S(O)}_m\text{NR}^9\text{R}^{10}$ ,
- (s)  $\text{NR}^9\text{C(=O)-R}^{12}$ ,
- (t)  $\text{C}_{1-7}$ alkyl which is optionally partially unsaturated and is optionally substituted by one or more  $\text{R}^{11}$ ,
- (u)  $\text{C}_{3-8}$ cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more  $\text{R}^{11}$ ,
- (v)  $-\text{C(O)H}$ , or
- (w)  $-\text{het}^1$ ;

 $\text{R}^9$  and  $\text{R}^{10}$  are independently

- (a) H,
- (b)  $\text{OR}^{12}$ ,
- (c) aryl optionally substituted by one or more  $\text{R}^{14}$ ,
- (d) heteroaryl optionally substituted by one or more  $\text{R}^{14}$ ,
- (e)  $\text{C}_{1-7}$ alkyl which is optionally substituted by one or more  $\text{R}^{11}$ ,
- (f)  $\text{C}_{3-8}$ cycloalkyl which is optionally substituted by one or more  $\text{R}^{11}$ ,
- (g)  $\text{(C=O)R}^{13}$ , or
- (h)  $\text{R}^9$  and  $\text{R}^{10}$  together with the nitrogen to which they are attached form morpholine, pyrrolidine, piperidine, thiazine, piperazine, each of the morpholine, pyrrolidine, piperidine, thiazine, piperazine being optionally substituted with  $\text{R}^{11}$ ;

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

 $R^{11}$  is

- (a) oxo,
- (b) phenyl optionally substituted by one or more  $R^{14}$ ,
- (c)  $OR^{12}$ ,
- (d)  $SR^{12}$ ,
- (e)  $NR^{12}R^{12}$ ,
- (f) halo,
- (g)  $CO_2R^{12}$ ,
- (h)  $CONR^{12}R^{12}$ ,
- (i)  $C_{1-7}$ alkyl which is optionally substituted oxo, halo,  $OR^{12}$ ,  $SR^{12}$ ,  $C_{1-7}$ alkyl, or  $NR^{12}R^{12}$  substituents, or
- (j)  $C_{3-8}$ cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more oxo, halo,  $OR^{12}$ ,  $SR^{12}$ ,  $C_{1-7}$ alkyl, or  $NR^{12}R^{12}$  substituents;

 $R^{12}$  is

- (a) H,
- (b)  $C_{1-7}$ alkyl which is optionally partially unsaturated and is optionally substituted by oxo, halo,  $C_{1-7}$ alkyl, or  $C_{1-7}$ alkoxy substituents,
- (c)  $C_{3-8}$ cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more oxo, halo,  $C_{1-7}$ alkyl, or  $C_{1-7}$ alkoxy substituents,
- (d) aryl optionally substituted by one or more halo,  $C_{1-7}$ alkyl, or  $C_{1-7}$ alkoxy substituents, or
- (e) heteroaryl optionally substituted by one or more halo,  $C_{1-7}$ alkyl, or  $C_{1-7}$ alkoxy substituents;

 $R^{13}$  is

- (a)  $C_{1-7}$ alkyl which is optionally substituted by one or more by oxo, halo, carboxyl,  $C_{1-7}$ alkyl, or  $C_{1-7}$ alkoxy substituents,
- (b)  $C_{3-8}$ cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more by oxo, halo,  $C_{1-7}$ alkyl, or  $C_{1-7}$ alkoxy substituents,
- (c) aryl optionally substituted by one or more halo,  $C_{1-7}$ alkyl, or  $C_{1-7}$ alkoxy substituents;

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

(d) heteroaryl optionally substituted by one or more halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy substituents,

(e) -C(O)OH

R<sup>14</sup> is

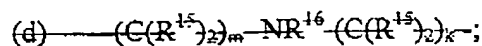
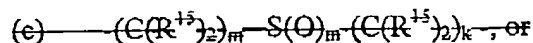
- (a) H,
- (b) halo,
- (c) C<sub>1-7</sub>alkyl,
- (d) OR<sup>12</sup>,
- (e) OCF<sub>3</sub>,
- (f) SR<sup>12</sup>,
- (g) S(O)<sub>m</sub>R<sup>13</sup>,
- (h) NR<sup>12</sup>R<sup>12</sup>,
- (i) NR<sup>12</sup>S(O)<sub>m</sub>R<sup>13</sup>,
- (j) NR<sup>12</sup>C(=O)OR<sup>13</sup>,
- (k) phenyl optionally substituted by halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy,
- (l) heteroaryl optionally substituted by halo, C<sub>1-7</sub>alkyl, or C<sub>1-7</sub>alkoxy,
- (m) cyano,
- (n) nitro,
- (o) CONR<sup>12</sup>R<sup>12</sup>,
- (p) CO<sub>2</sub>R<sup>12</sup>,
- (q) C(=O)R<sup>13</sup>,
- (r) C(=NOR<sup>12</sup>)R<sup>13</sup>,
- (s) S(O)<sub>m</sub>NR<sup>12</sup>R<sup>12</sup>,
- (t) NR<sup>9</sup>C(=O)-R<sup>12</sup>,
- (u) C<sub>1-7</sub>alkyl which is optionally partially unsaturated and is optionally substituted by oxo, halo, OR<sup>12</sup>, SR<sup>12</sup>, C<sub>1-7</sub>alkyl, or NR<sup>12</sup>R<sup>12</sup> substituents, or
- (v) C<sub>3-8</sub>cycloalkyl which is optionally partially unsaturated and is optionally substituted by oxo, halo, OR<sup>12</sup>, SR<sup>12</sup>, C<sub>1-7</sub>alkyl, or NR<sup>12</sup>R<sup>12</sup> substituents;

X is

- (a)  $\text{---}(\text{C}(\text{R}^{15})_2)_n\text{---}$
- (b)  $\text{---}(\text{C}(\text{R}^{15})_2)_m\text{---O---}(\text{C}(\text{R}^{15})_2)_k\text{---}$

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

Each  $R^{15}$  is independently

- (a) H,
- (b)  $OR^{11}$ ,
- (c) Oxo,
- (d)  $C_{1-7}$  alkyl which is optionally substituted by one or more ~~by one or~~ more  $R^{11}$  substituents,

(e)  $C_{3-8}$  cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more ~~by one or more~~  $R^{11}$  substituents,

- (f) aryl optionally substituted by one or more  $R^8$ , or
- (g) heteroaryl optionally substituted by one or more  $R^8$ ;

 $R^{16}$  is

- (a) H
- (b)  $OR^{12}$ ,
- (c)  $(C=O)R^{13}$ ,
- (d)  $(C=O)OR^{13}$ ,
- (e)  $(C=O)NR^9R^{10}$ ,
- (f)  $S(O)_mR^{13}$ ,
- (g)  $S(O)_mNR^9R^{10}$ ,
- (h)  $C_{1-7}$  alkyl which is optionally substituted by one or more  $R^{11}$  substituents,
- (i)  $C_{3-8}$  cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more  $R^{11}$  substituents;

- (j) aryl optionally substituted by one or more  $R^8$ , or
- (k) heteroaryl optionally substituted by one or more  $R^8$ ;

 $R^{17}$  is

- (a) H,
- (b) -OH, and
- (c)  $C_{1-4}$  alkyl;

 $R^{19}$  is

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

(a) H,  
 (b)  $OR^{11}$ ,  
 (c) Oxo,  
 (d)  $C_{1-7}$  alkyl which is optionally substituted by one or more ~~by one or~~  
~~more~~- $R^{11}$  substituents,

(e)  $C_{3-8}$ cycloalkyl which is optionally partially unsaturated and is  
 optionally substituted by one or more ~~by one or more~~- $R^{11}$  substituents,

(f) aryl optionally substituted by one or more  $R^8$ , or  
 (g) heteroaryl optionally substituted by one or more  $R^8$ ;

 $R^{20}$  is

(a) H,  
 (b)  $C_{1-7}$ alkyl which is optionally partially unsaturated and is optionally  
 substituted by one or more  $R^{11}$ ,

(c)  $C_{3-8}$ cycloalkyl which is optionally partially unsaturated and is  
 optionally substituted by one or more  $R^{11}$ ,

(d) aryl optionally substituted by one or more  $R^8$ ,  
 (e) heteroaryl optionally substituted by one or more  $R^8$ , or  
 (f)  $R^{20}$  and  $R^{19}$ , taken together, form- $CH_2$ -;

wherein, "aryl" denotes a phenyl radical or an ortho-fused bicyclic  
 carbocyclic radical having about nine to ten ring atoms in which at least one ring is  
 aromatic;

wherein, "heteroaryl" encompasses a radical attached via a ring carbon or  
 ring nitrogen of a monocyclic aromatic ring containing five or six ring atoms consisting  
 of carbon and 1, 2, 3, or 4 heteroatoms, selected from oxygen (-O-), sulfur (-S-),  
 oxygenated sulfur such as sulfinyl ( $S=O$ ) and sulfonyl ( $S(=O)_2$ ), or nitrogen  $N(Z)$   
 wherein Z is absent or is H, O,  $C_{1-4}$ alkyl, phenyl or benzyl, or a radical of an ortho-fused  
 bicyclic heterocycle of about eight to ten ring atoms derived therefrom;

het<sup>1</sup> is a C- or N- linked five- (5), six- (6), seven- (7), or eight- (8)  
 membered mono- or bicyclic ring, each mono- or bicyclic ring being fully saturated or  
 partially unsaturated, and having 1-4 heteroatoms selected from the group consisting of  
 oxygen, sulfur, and nitrogen; het<sup>1</sup> being optionally substituted by 1-2 substituents



USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

selected from C<sub>1</sub>-C<sub>4</sub>alkyl, amino, C<sub>1</sub>-C<sub>4</sub>alkylamino, C<sub>1</sub>-C<sub>4</sub>alkyloxy, halogen -CN, =O, =S;

each k is independently 0, 1, or 2;

each m is independently 0, 1, or 2;

each n is independently 1, 2, or 3; and

provided that

when each R<sub>4</sub> is H, that R<sub>1</sub> and R<sub>2</sub> are not simultaneously H, CN, or -C(O)-OCH<sub>3</sub> or that R<sub>1</sub> is not CN and R<sub>2</sub> is not -C(O)-OC<sub>1-4</sub>alkyl;

when the compound is 1,2,4,4a-Tetrahydro-cis-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione that the compound is enantiomerically enriched (-) form of (2R,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione; and

the compound is not 2,3,4,4a-tetrahydro-1',3'-dimethylspiro[1H 1-methylpyrazino[1,2-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2'4'6'(1'H, 3'H)-trione.

2. (Original) The compound of claim 1, wherein each R<sup>4</sup> is independently

- (a) H,
- (b) halo,
- (c) SR<sup>12</sup>,
- (f) S(O)<sub>m</sub>R<sup>13</sup>,
- (g) NR<sup>9</sup>R<sup>10</sup>,
- (h) NR<sup>9</sup>S(O)<sub>m</sub>R<sup>13</sup>,
- (i) NR<sup>9</sup>C(=O)OR<sup>13</sup>,
- (j) phenyl optionally substituted by one or more R<sup>8</sup>,
- (k) heteroaryl optionally substituted by one or more R<sup>8</sup>,
- (l) cyano,
- (m) nitro,
- (n) CONR<sup>9</sup>R<sup>10</sup>,
- (o) CO<sub>2</sub>R<sup>12</sup>,
- (p) C(=O)R<sup>13</sup>,
- (q) C(=NOR<sup>12</sup>)R<sup>13</sup>,

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

- (s)  $\text{NR}^9\text{C}(=\text{O})\text{-R}^{12}$ ,
- (t)  $\text{C}_{1-7}$ alkyl which is optionally partially unsaturated and is optionally substituted by one or more  $\text{R}^{11}$ , or
- (u)  $\text{het}^1$  optionally substituted by one or more  $\text{R}^8$ .

3. (Original) The compound of claim 2, wherein each  $\text{R}^4$  is independently selected from  $\text{NO}_2$ , H, Br, F,  $\text{CF}_3$ , CN,  $\text{NH}_2$ ,  $-\text{C}(\text{O})\text{-OCH}_3$ ,  $-\text{S-CH}_3$ ,  $-\text{S}(\text{O})_2\text{-CH}_3$ ,  $-\text{N}(\text{OCH}_3)\text{-CH}_3$ ,  $-\text{NH-C}(\text{O})\text{-O-}t\text{butyl}$ ,  $-\text{NH-C}(\text{O})\text{-CH}_3$ , heteroaryl optionally substituted by one or more  $\text{R}^8$ ,  $\text{het}^1$  optionally substituted by one or more  $\text{R}^8$ ,  $-\text{S}(\text{O})_2\text{-CH}_3$ , or phenyl optionally substituted by one or more of  $\text{NO}_2$ , Cl, F,  $-\text{OCH}_3$ , and  $-\text{OCF}_3$ .

4. (Original) The compound of claim 1, wherein each  $\text{R}^3$  is H.

5. (Original) The compound of claim 1, wherein  $\text{R}^1$  is  $-\text{C}(\text{O})\text{R}^6$ .

6. (Original) The compound of claim 1, wherein  $\text{R}^2$  is  $-\text{C}(\text{O})\text{R}^7$ .

7. (Original) The compound of claim 6, wherein  $\text{R}^1$  is  $-\text{C}(\text{O})\text{R}^6$ .

8. (Original) The compound of claim 7, wherein  $\text{R}^6$  and  $\text{R}^7$  form  $-\text{N}(\text{R}^{17})\text{-C}(\text{O})\text{-N}(\text{R}^{17})\text{-}$  or  $-\text{N}(\text{R}^{17})\text{-C}(\text{S})\text{-N}(\text{R}^{17})\text{-}$ .

9. (Canceled)

10. (Currently Amended) The compound of claim 1, wherein X is  $-\text{C}(\text{R}^{15})_2\text{-O-C}(\text{R}^{15})_2\text{-}$  or  $-\text{C}(\text{R}^{15})_2\text{-NR}^{16}\text{-C}(\text{R}^{15})_2\text{-}$ .

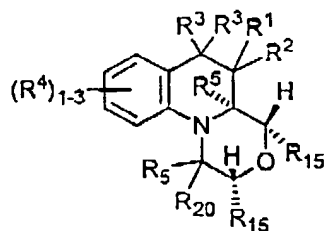
11. (Original) The compound of claim 10, wherein each  $\text{R}^{15}$  is independently H,  $\text{C}_{1-7}$ alkyl optionally substituted by one or more  $\text{R}^{11}$  substituents.

12. (Currently Amended) The compound of claim 11, wherein X is  $-\text{C}(\text{H})(\text{C}_{1-4}\text{alkyl})\text{-O-C}(\text{H})(\text{C}_{1-4}\text{alkyl})\text{-}$  or  $-\text{C}(\text{H})(\text{C}_{1-4}\text{alkyl})\text{-NR}^{16}\text{-C}(\text{H})(\text{C}_{1-4}\text{alkyl})\text{-}$ .

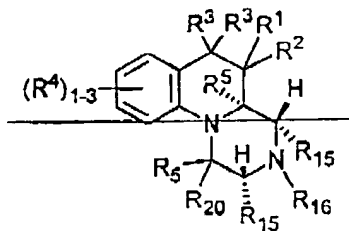
13. (Currently Amended) The compound of claim 10, wherein the compound has the formula of

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

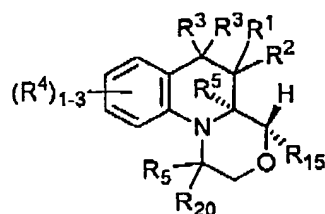


or

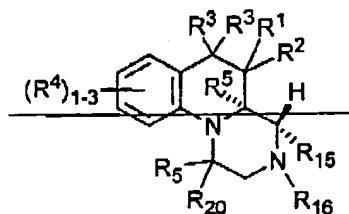
and each R<sub>15</sub> is

independently (b), (c), (d), (e), (f), or (g).

14. (Currently Amended) The compound of claim 10, wherein the compound has the formula of



or

and each R<sub>15</sub> is

independently (b), (c), (d), (e), (f), or (g).

15. (Original) The compound of claim 10, wherein R<sup>16</sup> is (C=O)OR<sup>13</sup> or C<sub>1-7</sub> alkyl.

16. (Original) The compound of claim 1, wherein each R<sup>5</sup> is independently H or C<sub>1-7</sub>alkyl.

17. (Currently Amended) A compound selected from  
 (2R,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;  
 1,2,4,4a-Tetrahydro- 2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;  
 8-Bromo-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;  
 8-Fluoro-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-trifluoromethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

1,1',2, 3',4,4',4a, 6'-Octahydro-2,4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-8-carbonitrile;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-carboxamidespiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

1,2,4,4a-Tetrahydro-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

~~8-Bromo-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]piperazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;~~

1,2,4,4a-Tetrahydro-1,4a-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

8-Bromo-1,2,4,4a-tetrahydro-cis-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-4'-thioxo-2',6' (1' H,3' H)-dione;

8-Bromo-1,2,4,4a-tetrahydro-cis-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' methyl, 3' methyl)-trione;

*N*-[1,1',2,3',4,4',4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinolone-5(6H),5'(2' H)-pyrimidin-8-yl]acetamide;

*tert*-butyl 1,1',2, 3',4,4',4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinolone-5(6H),5'(2' H)-pyrimidin-8-yl]carbamate;

8-Amino-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinolone-5(6H),5'(2' H)-pyrimidine]-2',4',6'(1' H,3' H)-trione monohydrochloride;

9-Bromo-1,2,4,4a-tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

8-Acetyl-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

8-Ethanone-O-methyloxime-1-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-(methylsulfonyl)spiro[[1,4]oxazino [4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-(methylsulfinyl)spiro[[1,4]oxazino [4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-(methylthio)spiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*methyl*,3'*methyl*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*, 3'*methyl*)-trione;

1,2, 4,4a-Tetrahydro-4-methyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2-methyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*s*)-trione;

~~2,3,4,4a-Tetrahydro 1',3,3'-trimethylspiro[1*H*-pyrazino[1,2-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;~~

~~2,3,4,4a-Tetrahydro 3-methylspiro[1*H*-pyrazino[1,2-*a*]quinoline 5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;~~

~~1,1-Dimethylethyl 1,1',2,3',4',4a,6'-octahydro-8-nitro-2',4',6'-trioxospiro[3*H*-pyrazino[1,2-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-3-carboxylate;~~

~~1,1-Dimethylethyl 8-cyano-1,1',2,3',4',4a,6'-octahydro-2',4',6'-trioxospiro[3*H*-pyrazino[1,2-*a*]quinoline 5(6*H*),5'(2'*H*)-pyrimidine]-3-carboxylate;~~

1,1',2'3'4'4'-Hexahydro-2',4'-dimethyl-1,3-dioxospiro[2*H*-indene-2,5'(6'*H*)-[1,4]oxazino[4,3-*a*]quinoline]-8'-carbonitrile;

1,2,4,4a-Tetrahydro-2,4-dimethyl[1,4]oxazino[4,3-*a*]quinoline-5,5,8(6*H*)-tricarbonitrile;

8-Bromo-1,2,4-4a-tetrahydro-2,4-dimethyl[1,4]oxazino[4,3-*a*]quinoline-5,5(6*H*)-dicarbonitrile;

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

~~2,3,4,4a-Tetrahydro-3-methyl-8-nitro-2'-thioxospiro[1H-pyrazino[1,2-a]quinoline-5(6H),5'(2'H)-pyrimidine]-4',6'(1'H,3'H)-dione;~~

9-(4-Chlorophenyl)-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-[4-(trifluoromethoxy)phenyl]spiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-9-(methoxyphenyl)-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

9-(3-Chloro-4-fluorophenyl)-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-(3-nitrophenyl)spiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

1,1',2,3',4,4',4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidin]-9-yl]benzonitrile;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-[4-(methylsulfonyl)phenyl]spiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-(4-pyridinyl)spiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

Methyl-1,1'-2,3',4,4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-9-carboxylate; and

Methyl-1,1'-2,3',4,4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-8-carboxylate;

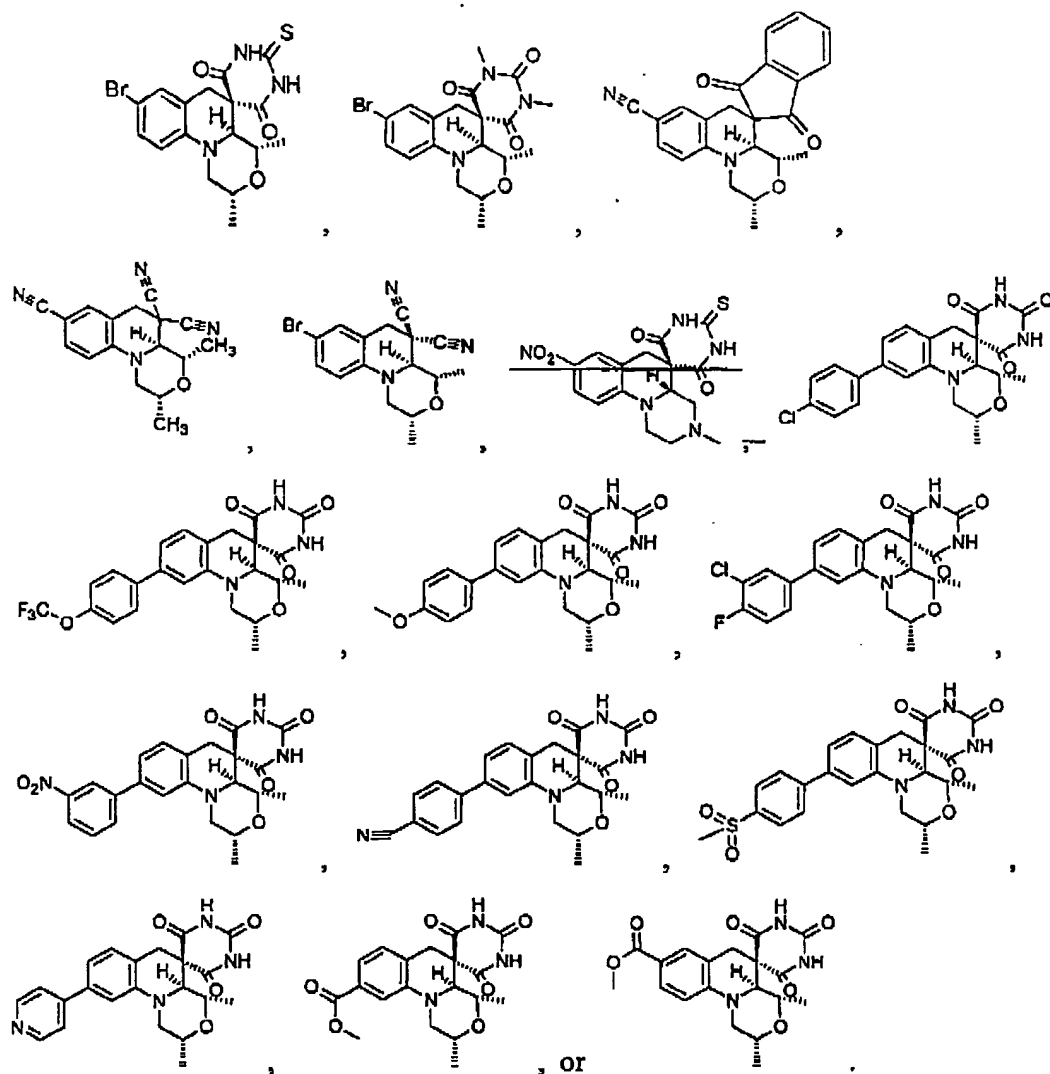
~~1,2,3,3',4,4',4a,6'-Octahydro-2',4',6'-trioxospiro[1H-pyrazino[1,2-a]quinoline-5(6H),5'(2'H)-pyrimidine-8-carbonitrile monohydrochloride; and~~

~~2,3,4,4a-Tetrahydro-8-nitrospiro[1H-pyrazino[1,2-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione monohydrochloride.~~

18. (Currently Amended) A compound selected from

USSN: 10/677,551

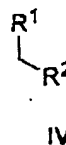
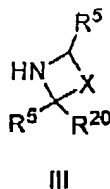
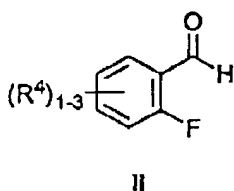
Ref. No. 27712 (formerly 01337.US1)



19. (Currently Amended) A method of synthesizing compounds of claim 1 having formula I, comprising reacting an amine of the formula III with a fluoroaldehyde of the formula II in a polar, aprotic solvent, followed by methylenation with a compound of the formula IV, and thermal rearrangement in a polar, protic solvent, an aprotic solvent, or a nonpolar solvent system including  $\text{ZnCl}_2$ .

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)



wherein, X, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, and R<sup>20</sup> are as defined in claim 1 above.

20. (Currently Amended) A method for the treatment of bacterial microbial infections in mammals comprising administration of an effective amount of compound of claim 1 to said mammal.

21. (Original) The method of claim 20 wherein said compound of claim 1 is administered to the mammal orally, parenterally, transdermally, or topically in a pharmaceutical composition.

22. (Original) The method of claim 20 wherein said compound is administered in an amount of from about 0.1 to about 100 mg/kg of body weight/day.

23. (Original) The method of claim 20 wherein said compound is administered in an amount of from about 1 to about 50 mg/kg of body weight/day.

24. (Original) A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

25. (Currently Amended) A pharmaceutical composition comprising one or more compounds of claim 1 and a pharmaceutically acceptable carrier.

26. (Original) The composition of claim 25 wherein the composition comprises an enantiomerically enriched form of a compound of formula I.

27. (Original) The composition of claim 26, wherein the composition comprises at least 50% of one enantiomer of a compound of formula I relative to the other enantiomer of the compound.



USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

28. (Original) The compositions of claim 27, wherein the composition comprises at least 80% of one enantiomer of a compound of formula I relative to the other enantiomer of the compound.

29. (Original) The compositions of claim 27, wherein the composition comprises at least 90% of one enantiomer of a compound of formula I relative to the other enantiomer of the compound.

30. (Currently Amended) A compound selected from  
(2S,4R,4aR)-4-isopropyl-2-methyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;  
(2R,4S,4aS)-2,4-diethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;  
(2R,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;  
(2R,4S,4aS)-8-acetyl-9,10-difluoro-2,4-dimethyl-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;  
(2R,4S,4aS)-10-fluoro-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;  
(2R,4S,4aS)-2,4-dimethyl-8-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;  
1,2,4,4a-Tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;  
(2S,4R,4aR)-2-isopropyl-4-methyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;  
(2S,4R,4aR)-2-isopropyl-4-methyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;  
(2R,4S,4aS)-2,4-diisopropyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;  
(2R,4S,4aS)-2,4-dimethyl-8-(3-methyl-1,2,4-oxadiazol-5-yl)-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

USSN: 10/677,551

Ref. No. 27712 (formerly 01337.US1)

(2S,4R,4aR)-8-acetyl-10-fluoro-2,4-dimethyl-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

~~(2'R,4'S,4a'S)-2',4'-dimethyl-8'-nitro-1',2',4',4a'-tetrahydro-2'H,6'H-spiro[pyrimidine-5,5' [1,4]thiazino[4,3-a]quinoline]-2,4,6(1'H,3'H)-trione;~~

8-bromo-2,4-dimethyl-10-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2R,4S,4aS)-2,4-dimethyl-8-(5-methyl-1,2,4-oxadiazol-3-yl)-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2S,4S,4aS)-4-methyl-8-nitro-2-(trifluoromethyl)-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

4-azido-3-iodobenzyl (2R,4S,4aS)-2,4-dimethyl-2',4',6'-trioxo-1,1',2,3',4,4',4a,6'-octahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-8-carboxylate; or

(2S,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione.